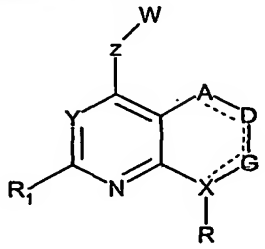
Claims

1. Compounds of formula (I) including stereoisomers, prodrugs and pharmaceutically acceptable salts or solvates thereof



(I)

wherein

the dashed line may represent a double bond;

R is aryl or heteroaryl, each of which may be substituted by 1 to 4 groups J selected from:

halogen, C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, halo C1-C6 alkoxy, $-C(O)R_2$, nitro, hydroxy, $-NR_3R_4$, cyano, and or a group Z;

R_1 is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 thioalkyl, C2-C6 alkenyl, C2-C6 alkynyl, halo C1-C6 alkyl, halo C1-C6 alkoxy, halogen, NR_3R_4 or cyano;

R_2 is a C1-C4 alkyl, $-OR_3$ or $-NR_3R_4$;

R_3 is hydrogen or C1-C6 alkyl;

R_4 is hydrogen or C1-C6 alkyl;

R_5 is a C1-C6 alkyl, halo C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkoxy, C3-C7 cycloalkyl, hydroxy, halogen, nitro, cyano, $-NR_3R_4$; $-C(O)R_2$;

R_6 is a C1-C6 alkyl, halo C1-C6 alkyl, C1-C6 alkoxy, halo C1-C6 alkoxy, C3-C7 cycloalkyl, hydroxy, halogen, nitro, cyano, $-NR_3R_4$; $-C(O)R_2$;

R_7 is hydrogen, C1-C6 alkyl, halogen or halo C1-C6 alkyl;

R_8 is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_9 is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_{10} is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_{11} is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_{12} is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_{13} is hydrogen, C3-C7 cycloalkyl, C1-C6 alkyl, C2-C6 alkenyl, C2-C6 alkynyl, NR_3R_4 or cyano;

R_{14} is R_3 or $-C(O)R_2$;

D is CR_8R_9 or is CR_8 when double bonded with G or A;

G is $CR_{10}R_{11}$ or is CR_{10} when double bonded with D or is CR_{10} when double bonded with X when X is carbon;

A is $CR_{12}R_{13}$ or is CR_{12} when double bonded with D;

X is carbon or nitrogen;

Y is nitrogen or $-CR_7$;

W is a 4-8 carbocyclic membered ring, which may be saturated or may contain one to three double bonds, and

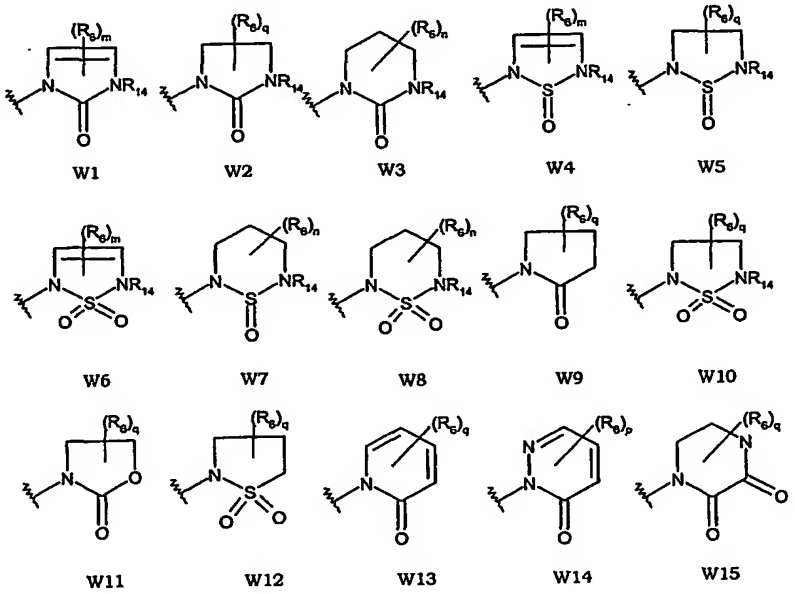
in which:

- one carbon atom is replaced by a carbonyl or $S(O)_m$; and
- one to four carbon atoms may optionally be replaced by oxygen, nitrogen or NR_{14}, $S(O)_m$, carbonyl, and such ring may be further substituted by 1 to 8 R_6 groups;

Z is a 5-6 membered heterocycle or a phenyl, which may be substituted by 1 to 8 R_5 groups;

m is an integer from 0 to 2.

2. Compounds according to claim 1, in which W is selected among the following groups:



in which:

W1 represents a 1,3-dihydro-2H-imidazol-2-one derivative;

W2 represents a imidazolidin-2-one derivative;

W3 represents a tetrahydropyrimidin-2(1H)-one derivative;

W4 represents a 2,5-dihydro-1,2,5-thiadiazole 1-oxide derivative;

W5 represents a 1,2,5-thiadiazolidine 1-oxide derivative;

W6 represents a 2,5-dihydro-1,2,5-thiadiazole 1,1-dioxide derivative;

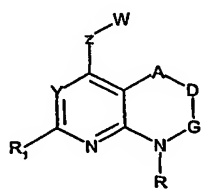
W7 represents a 1,2,6-thiadiazinane 1-oxide derivative;

W8 represents a 1,2,6-thiadiazinane 1,1-dioxide derivative;

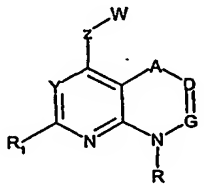
W9 represents a pyrrolidin-2-one derivative;

W10 represents a 2,5-dihydro-1,2,5-thiadiazolidine 1,1-dioxide derivative;
W11 represents a 1,3-oxazolidin-2-one derivative;
W12 represents a isothiazolidine 1,1-dioxide derivative;
W13 represents a 2(1H)-pyridinone derivative;
W14 represents a 3(2H)-pyridazinone;
W15 represents a 2,3-piperazinedione derivative;
and q is an integer from 0 to 4, n is an integer from 0 to 6, p is an integer from 0 to 3 and m, R_6 and R_{14} are defined as in claim 1.

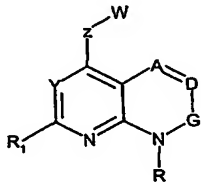
3. Compounds accordjng to claims 1 and 2 of formula (Ia), (Ib), (Ic), (Id), and (Ie),



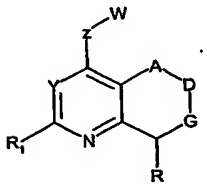
(Ia)



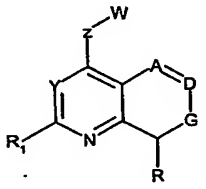
(Ib)



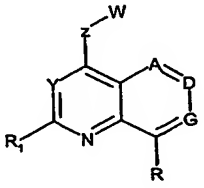
(Ic)



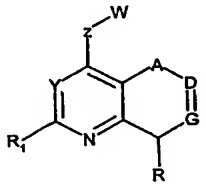
(Id)



(Ie)



(If)

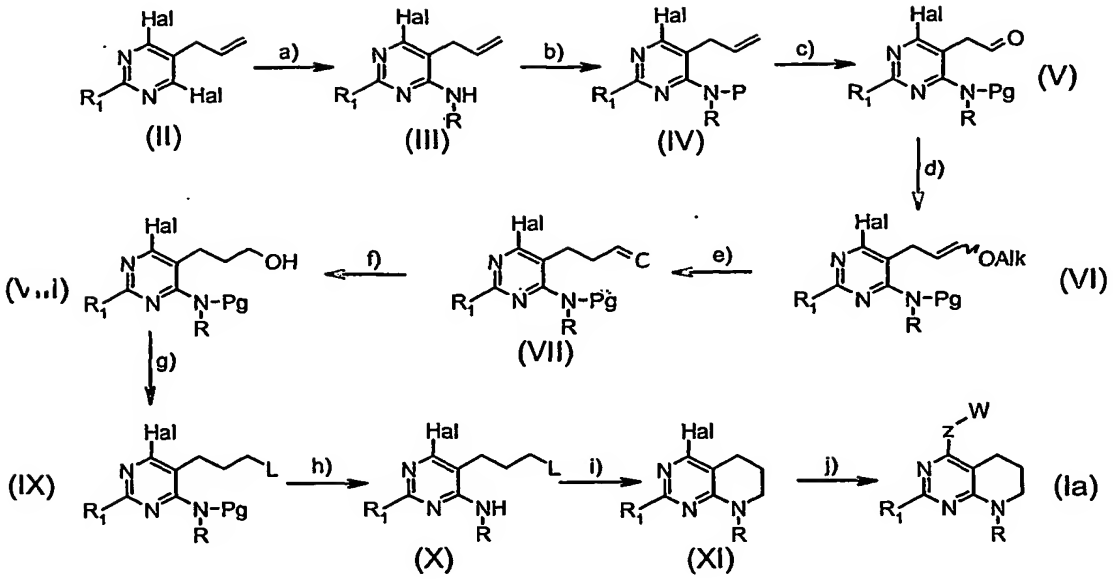


(Ig)

in which R, R_1, Z, Y, W, A, D, G are defined as in claim 1 and 2.

4. Compounds according to anyone of claims from 1 to 3, selected from the following group:
1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidin-4-yl]-1*H*-pyrazol-3-yl}-2-imidazolidinone;
1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydro-4-quinazolinyl]-1*H*-pyrazol-3-yl}-2-imidazolidinone;
1-{1-[8-(2,4-dichlorophenyl)-2-methyl-5,6,7,8-tetrahydro-1,8-naphthyridin-4-yl]-1*H*-pyrazol-3-yl}-2-imidazolidinone.

5. Process for preparing compounds of formula (Ia) comprising the following steps:



in which

step a stands for the nucleophilic substitution with a suitable amine (such as a substituted aniline) of compounds of formula (II), in basic conditions (such as sodium hydride in a polar aprotic solvent) to give compounds (III);

step b stands for the protection of the amino group with a suitable protecting group (such as a BOC group);

step c stands for the oxidation of the double bond with a suitable oxidizing agent (such as ozone in a polar protic solvent) to give the aldehyde of compounds (V);

step d + e stands for formation of the aldehyde group of compounds (VII) through formation of the enol ether by Wittig reaction in the usual conditions, followed by acid hydrolysis (step e);

step f stands for the reduction of the aldehyde group of compounds (VII) to the alcohol of compounds (VIII) with a suitable reducing agent (such as sodium borohydride);

step g stands for the conversion of the alcohol of compounds (VIII) into a suitable leaving group (such as, for example, a halogen or reactive residue of sulphonic acid (e.g. mesylate, tosylate), preferably mesylate);

step h stands for the deprotection of the amino group of compounds (IX);

step i stands for the intramolecular cyclization to give the cyclized compounds (X)

step j stands for conversion of the halogen derivative, preferably chloride, into compounds (Ia), by reaction with the suitable reactive -Z-W derivative, in basic conditions (such as, for example, sodium hydride in a polar solvent).

6. The use of a compound according to anyone from claim 1 to 4, in the preparation of a medicament for use in the treatment of conditions mediated by CRF (corticotropin-releasing factor).

7. The use of a compound according to claim 6, in the preparation of a medicament for use in the treatment of depression and anxiety.

8. The use of a compound according claim 6, in the preparation of a medicament for use in the treatment of IBS (irritable bowel disease) and IBD (inflammatory bowel disease).

9. A compound according to anyone from claim 1 to 4, for use in the treatment of conditions mediated by CRF (corticotropin-releasing factor).

10. A pharmaceutical composition comprising a compound of anyone from claim 1 to 4, in admixture with one or more physiologically acceptable carriers or excipients.

11. A method for the treatment of a mammal, including man, in particular in the treatment of conditions mediated by CRF (corticotropin-releasing factor), comprising administration of an effective amount of a compound according to any of claims from 1 to 4.

12. A method, according to claim 11, in the treatment of depression and anxiety, comprising administration of an effective amount of a compound according to any of claims 1 to 4.

13. A method, according to claim 11, in the treatment of IBS (irritable bowel disease) and IBD (inflammatory bowel disease), comprising administration of an effective amount of a compound according to any of claims 1 to 4.